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EDITORIAL

DEPARTMENT STORE HYPNOTICS

MEDICAL and pharmaceutical literature has frequently referred, during the course of the last few years, to the evils attendant upon unregulated and unwise self-medication with hypnotic and analgesic drugs.

The synthetics of the malonyl-urea or barbituric acid group, such as the official barbital and phenyl-barbital and a host of their trade-marked kindred, are charged with being the worst offenders—and particularly so because of their alleged habit-forming properties.

For several reasons, the extent of the wide-open traffic in these drugs is increasing daily, and only in a few states and sections is their sale in any way restricted.

The professions, as is so often the case, gave them their start in sales success and continue today, to abet them.

Dentists dispense, on the slightest hint, their labelled packs of pain dispelling pellets, and the patient may readily buy them again at any willing establishment. Doctors prescribe them, under readily readable names that anyone may well remember, and that in end will recommend themselves to sleepy but sleepless victims.

Department stores and drug shops, and sometimes even the old line pharmacy freely sell these harmful remedies, like any cut price medicine, to all who come to buy them.

The jaded, nervous woman, whose short nights are long and whose long days are short soon finds that "Sleep, the soother of hearts"—can be bought like ribbon at the counter—only that this is as "poppied sleep"—hired, hurt and haunted.

The worried business man, in the red all day, sleeps in the blue with barbital, yet finds that this death of his each day's life sinks his depression still deeper.

The whole thing is wrong!! Valuable drugs these are, when properly administered. In an intelligent physician's hand they are a blessing and boon, but they are much too dangerous for uncontrolled and indiscriminate practice. They should certainly not be as available as air to anyone who wants them!

Pharmacists welcomed Federal control of opium and coca traffic and none of the professions has cooperated more fully with the Harrison Law provisions.

They will be equally glad to find a way to control the dispensing and sale of these obnoxious hypnotics.

IVOR GRIFFITH.

The scholar must with his classical spirit come into the crowded city and there recognize and enhalo the work of those who have reared their zikkurats higher than those of the inhabitants of Ur, in order to have wider commerce with men. There was never greater need of this classical spirit in setting the standards for the new creation—for synthetic culture. To it even the merchants in the agora and the workmen at their trades must look, not to seek out for them words modulated to Greek lyres or Latin lutes but to learn thoroughly the measure and poetry of true life.

Matthew Arnold, it will be remembered, defined culture as "the criticism of life by gifted men alive and active with extraordinary power at an unusual number of points." But that is only its analytical function, its initial definition, the first stage of culture. If it stops there, it is a futile activity, unless other gifted men "alive and active with extraordinary power at an unusual number of points" synthesize into new forms of life and higher culture the elements torn apart by criticising analysis. It is upon the second stage that we are entering in education, though perhaps we have not gone far enough in analysis to furnish much material for the synthetic specialists. (John H. Finley.)

ORIGINAL ARTICLES

AN ELECTRICAL METHOD FOR CHECKING PHYSIOLOGICAL SALT SOLUTION*

By J. Howard Graham†

"SALINE", or physiological salt solution (1) is prepared daily in hundreds of liters for our hospitals and it is very essential that it be a sterile solution of 8.5 g. of pure sodium chloride per 1000 ml., an 0.85 per cent. solution. Scientists know only too well the dire results that may result from the use of anything but the correct percentage of salt. We maintain that this solution should be prepared by thoroughly competent persons qualified for this service, and it should be checked by others.

Any one of several chemical methods offer themselves as rapid checks upon the percentage strength of solution; but electrical methods are rapidly replacing the older chemical methods for determining the soluble salt contents of solutions. Note for instance the excellent work being done by the U. S. Department of Agriculture (2) in investigating saline contents of soils by electrical methods. In this work some form of Wheatstone bridge is used with conductivity cells properly adapted for this type of investigation.

Without going into details of apparatus and method, both of which are generously furnished by supply houses for electrical instruments, one requires a Wheatstone bridge, a "U" type conductivity cell, dial resistance box, buzzer, telephone head band and cord, dry cell and contact key. With these, specific conductivity or specific resistivity, one the reciprocal of the other, can be easily determined, or, using constant temperature at all times, and the cell factor, numbers for comparison may be obtained suitable to the purpose of any investigator. The curve which we have plotted herewith shows how sufficiently accurate check information may be obtained. Temperatures *must* be taken into consideration, because resistance varies inversely as the temperature, and for comparable results operating conditions must be maintained uniform.

*Read at Fifty-seventh Annual Meeting of Pennsylvania Pharmaceutical Association, June 21, 1934.

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Working with the platinized electrodes kept at a definite distance apart, with the use of salines of approximately the same normality, with the maintenance of a constant temperature, if "C" is the cell factor and "R_m" the measured resistance in ohms, then "R_s" is the specific resistance, and "K" is specific conductance (the reciprocal of specific resistance) and we have:

$$\frac{C}{R_m} \text{ equals } K \qquad Rs \text{ equals } \frac{R_m}{C}$$

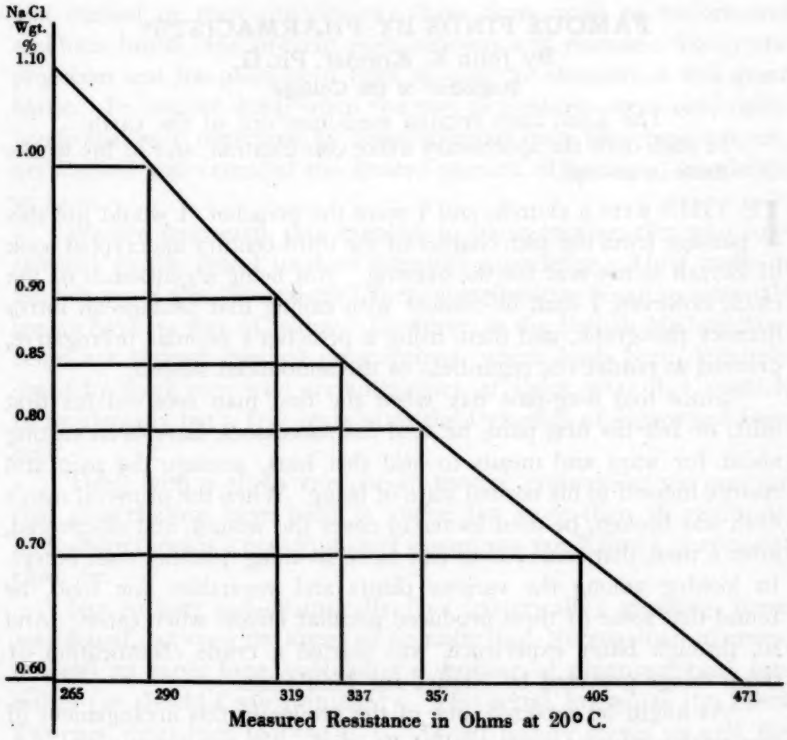
However, for comparative results and check purposes, the information supplied by the attached graph should be all that is necessary. The apparatus, which may be of the simplest type, can be kept set up so that within one or two minutes time, the physiological salt solution can be checked for its saline content, and the actual per cent. contents be determined from the graph.

Per Cent. Saline	*Ohms R_m*	*Temp. Deg. C.*
0.60	471	20
0.70	405	20
0.80	357	20
0.85	337	20
0.90	319	20
1.00	290	20
1.10	265	20

We urge a close check upon the physiological salt solution, and recommend the electrical method. This check work is a part of the laboratory work of our students in the pharmacy.

REFERENCES

1. *U. S. Pharmacopœia X*, 226 (1926).
2. U. S. Department Agriculture Circular No. 232 (1932).


Na Cl Wgt. %
1.10
1.00
0.90
0.85
0.80
0.70
0.60
265
290
319
337
357
405
471
Measured Resistance in Ohms at 20° C.

FAMOUS FINDS BY PHARMACISTS*

By John E. Kramer, Ph. G.
Registrar of the College

"The Lord hath created medicines out of the earth. . . . In such doth the apothecary make continuation, and of his works there is no end."

IF THIS were a church, and I were the preacher, I would use this passage from the 38th chapter of the third century apocryphal book of Serach as my text for the evening. Not being a gentleman of the cloth, however, I shall be content with calling that passage an introductory paragraph, and then, using a preacher's popular prerogative, proceed to ramble on, regardless of the announced subject.

Since that long-past day when the first man received his first hurt, or felt his first pain, he, and his successors, have been casting about for ways and means to heal that hurt, assuage the pain and restore himself to his normal state of being. When the primeval man's flesh was broken, he used leaves to cover the wound, and discovered, after a time, that some leaves had more soothing qualities than others. In looking among the various plants and vegetables for food, he found that some of them produced peculiar effects when eaten. And so, through bitter experience, was started a crude classification of those things provided by Nature for Man's use.

As might be expected, one of the groups in this arrangement of the earth's resources was called "medicines", or whatever the primeval man grunted when he meant "drugs". And, as might also be expected, some of these medicines were good and some were bad. The true value of a medicine was found only through years of use, and a system of "handing down" from generation to generation.

It is natural to assume that all of this information about medicines was not common knowledge. Some folks had better memories than others. Some had more talent, skill and patience in the utilization of these healing medicines. Some kept their knowledge secret. The rest of the community, in time of illness and need, were, therefore, forced to appeal to this select group for assistance, and the medical profession came into being.

Those men who, in early days, took it upon themselves to be "medicine men", and those men who, in later times, have been chosen

*An Address given at the Philadelphia College of Pharmacy and Science.

and trained by their predecessors, have done much to restore and maintain health, and prevent pain, sickness and disease. Today the physician and the pharmacist fight shoulder to shoulder in this great battle. In ancient days, when the two professions were one, many handicaps were overcome by those splendid men who explored, experimented and extended the limited amount of accurate knowledge at hand.

We are interested, this evening, in those apothecaries who contributed to the grand total of scientific knowledge. How early in the history of this "mortal coil" these contributions began to materialize we have no way of telling. However, in the British Medical Museum are several medical prescriptions, which have been definitely dated by those men who are authorities, at about 3700 B. C., which is, incidentally but a few years after the Pyramids of Egypt had been built.

Thus, with a slight exercise in mental gymnastics, we can say that prescriptions have been in vogue for more than 56 centuries, and where there is a prescription, I assure you you'll find a pharmacist close by.

Not so long ago, historically (not hysterically) speaking, there was found, between the knees of an unearthed Necropolitan mummy, a scroll 22 yards long, containing a number of pharmaceutical formulas (or should I say formulæ?). This scroll, known as the Ebers Papyrus, dates back to 1552 B. C. If our history serves us well, the author of this scroll was a contemporary of Moses, the grand Biblical character.

In the Bible, too, in the book of Exodus, is a chapter containing a list of ingredients with the directions "to be mixed according to the art of the apothecary." Thus we see that in Biblical times the apothecary was an accepted and respected personage in the community.

True to my opening statement, I have been rambling on, but it was a premeditated ramble, in an endeavor to place before you a bit of historical background. Now, let us take up in chronological order those famous finds by pharmacists. Considering them in this order we avoid any discussion as to which of these discoveries are greater than others. All had some value, but their relative merits shall not enter into this discourse.

As the hour progresses you may think that I am reciting a list of "Believe-it-or-not's." It seems that the world has come to the

place where it takes a series of such cartoons, or "Strange-as-it-may-seem" pictures, to convey unusual facts. That being the case, here goes, and you can "believe-them-or-not," with apologies to Ripley.

Significant history in medicine and pharmacy seems to have made its first impressions in the fifth century, B. C., chiefly in the person of a great practitioner, teacher, writer and thinker,—Hippocrates. This most famous man did much to establish true facts in the healing arts, and during the ninety years of his life many false beliefs were overthrown. Hippocrates lives with us today in the form of the Hippocratic Oath, to which all reputable medical men subscribe, and consider themselves bound. Hippocrates wrote—

> I swear by Apollo the physician, and Æsculapius, and Hygeia, and Panacea, and all the gods and goddesses—and I make them my judges—that this, mine oath, I will fulfil as far as power and discernment shall be mine.
>
> Him who taught me this art I will esteem even as I do my parents; he shall partake of my livelihood, and, if in want, shall share my goods. I will regard his issue as my brothers and will teach them this art without fee or written engagements if they shall wish to learn it.
>
> I will give instruction by precept, by discourse, and in all other ways to my own sons, and to those of him who taught me, to disciples bound by written engagements and sworn according to medical law, and to no other person. So far as power and discernment shall be mine, I will carry out regimen for the benefit of the sick and will keep them from harm and wrong. To none will I give a deadly drug, even if solicited, nor offer counsel to such an end; likewise to no woman will I give a destructive suppository; but guiltless and hallowed will I keep my life and mine art. I will cut no one whatever for the stone, but will give way to those who work at this practice.
>
> Into whatsoever houses I shall enter, I shall go for the benefit of the sick, holding aloof from all voluntary wrong and corruption, including venereal acts upon the bodies of females and males, whether free or slaves. Whatsoever in my practice or not in my practice I shall see or hear amid the lives of men which ought not to be noised abroad—as to this I will keep silence, holding such things unfitting to be spoken.
>
> And now if I shall fulfil this oath and break it not, may the fruits of life and art be mine, may I be honored of all men for all time; the opposite if I shall transgress or be foresworn.

Quite idealistic, is it not? Yet, it has persisted through 24 centuries.

Passing quickly through the next few centuries, through the time of Christ, who, incidentally is quite often called the Divine Healer, and whose life is marked with many miraculous cures, we come to Cato and Pliny, Roman physicians of the first century, A. D., who are said to have introduced to an unsuspecting world castor oil, much to the disgust of, to date, 57 generations of children.

Next in the long line of men to be considered is Claudius Galenus, whose name time has shortened to Galen, and who was born in 130 A. D. in the Grecian town of Pergamum. Like Hippocrates, he was a prolific writer, experimenter and explorer. However, he took advantage of the accumulation of facts in the few hundred years since Hippocrates had held forth, and in his writings took exception, with proof, to many of the statements of his illustrious predecessor.

Galen is known as the father of experimental physiology. He was the first to attempt an intelligent, conscientious and complete probe of the body, its component parts and their functions. He made many statements concerning bone formation, blood circulation and other mortal matters. Very often he was wrong, but he was so strongly believed in that actual proof of his errors was not accepted by his many followers.

Galen had a fetish for drugs of vegetable origin, casting aside as useless the then known minerals. Even today, in pharmacy, preparations of vegetable origin are called galenicals. Probably the best known of his original compounds was Ceratum Infrigidans, the great-great-great-great-grandfather of our modern cold cream.

Shortly after Galen's time the so-called civilized portions of the world were changed to seething cauldrons of plunder and attack by barbarians. Then the long years of the Dark Ages set in, the Mohammedans "crept" in, Charlemagne "lept" in and William the Conqueror "swept" in. The Crusaders marched up the hill and then marched down again, the Magna Carta was signed, gunpowder was invented, and the world was more or less safe for democracy.

And so we find ourselves in the fifteenth century watching the alchemists in their vain attempts to transmute the baser metals into gold and silver. It was a far cry from 550 B. C., when Empedocles originated the idea that there were but four elements from which the entire universe was constructed, namely—earth, water, fire, and air. Yet the alchemists wasted much precious time in their futile efforts.

About this time there was holding forth in the scientific world one Philippus Aureolus Theophrastus Bombastus von Hohenheim,

who called himself Paracelsus for short. Paracelsus was a dashing, daring, physician-pharmacist, full of contempt for the accepted authorities of the past, present, and even the future and equally as full of rapt admiration for his own abilities. Just as Galen "debunked" Hippocrates, Paracelsus "debunked" them both, going so far as to publicly burn their works, and setting up a school of his own thought. Paracelsus' redeeming virtue was his utter disclaim for superstition, although some of his ideas were nothing but that. However, he led the way toward new thought by adding entirely from his own imagination, mercury, salt and sulphur to the four pseudo-elements, and by turning the alchemists' attention to the more worthwhile quest for new medical qualities in natural substances.

Huxley has stated that " the birth of science was the death of superstition," which statement works just as well in reverse. From this time on we note the real discoveries.

We note, too, another thing, here in the sixteenth and early seventeenth centuries. When these discoveries were made, they were kept secret as long as possible by their discoverers, who mixed, shall we say business, with genius, and divulged their secrets only to those who could sooth the pain of the parting of the brain-child from the parent with adequate balm of gilt.

For instance, Johann Rudolph Glauber, a German chemist, discovered, in 1603, in the waters of a Hungarian spring, a salt which had peculiar laxative qualities. With customary modesty he called it Glauber's Miraculous Salt. He even went to the trouble of synthesizing the salt, identified later as sodium sulphate. He made other discoveries and sold his secrets, probably to the highest bidder.

You can believe it or not, but the same compound, Glauber's Salt, is the basis of a proprietary article selling on the market this very moment for ten times its real worth and advertised as something to overcome that "tired feeling," and many other maladies.

Peter Seignette, a French pharmacist, discovered a marvelous salt with wonderful laxative and curative powers, and, in 1672, proclaimed it far and wide as the "salt of many virtues." Its composition, as you may have suspected, was a secret, and remained so for 60 years, when Baumé, another French pharmacist revealed the compound as sodium and potassium tartrate. It was earlier known as Seignette Salt, in honor of its discoverer, and later as Rochelle Salt, after the French town in which the discoverer lived.

Jacob Sylvius, a famous sixteenth century pharmaceutical commentator, originated our household aromatic spirits of ammonia, and

very "conscientiously" gave it a title containing his own name (Spiritus Carminativus Sylvius).

The late seventeenth century witnessed the life and works of Stephen Francis Geoffroy (1672-1731), another famous French pharmacist and research worker. It was his and his father's apothecary shop in which were held the first meetings of the Paris Academy of Sciences, even as, a little more than a century later, in 1815, the first meetings of the Academy of Natural Sciences were held in the drug store of Townsend Speakman, right here in Philadelphia.

The discoveries and conclusions of the early eighteenth century were not all correct, as exemplified by the famous phlogiston theory of Becher and Stahl, German chemists. They believed that substances either wholly or partly combustible, owed their property of combustion to one essential constituent, which they called phlogiston. This erroneous assertion very materially affected the researches of that day. Even as late as 1760 this theory was aided and abetted by J. G. Weiglieb, a German apothecary. Soon after, however, in 1775 and 1778, the phlogistonists were utterly routed by discoveries made by Lavoisier, the Frenchman. In the light of today's scientific knowledge, Becher, Stahl, Weiglieb and others of that school were blundering fools, working along lines that invariably led to wrong conclusions. Then, however, they were heroic pioneers, blazing paths through unexplored territory. Those who followed profited by their mistakes.

The eighteenth century also witnessed the life span of a brilliant chemistry and pharmacy student, inventor, teacher, author and lecturer. I speak of Antoine Baumé (1728-1804) mentioned before as revealer of the formula for Rochelle Salt. He took most of the repulsion from the theory that the more disgusting the medicine, the quicker and more efficient the cure. Baumé was a most versatile man, his accomplishments ranging from the invention of the hydrometer, which still bears his name, to the authorship of a book on grammar. He was recognized as France's most famous pharmacist of the time.

Another Frenchman of fame was Professor Venel of the widely known school of pharmacy at Montpelier, in the south of the land of vintage wines and champagnes. Venel became famous for something almost paradoxical and surely less innocuous than wines,—soda water. In 1750 he presented a paper to the French Academy of Sciences on carbonated water and was the first to make this substance.

Priestly, whom we shall mention later, also came across this substance independently in some work he was doing in 1767, but neither man realized the commercial potentialities of his find. Other more commercially minded men perfected the flavored soda water idea, and patented it in 1810.

It was another French pharmacist, Elias Durand, who, after serving as pharmacist in Napoleon's Army, emigrated to America, settled here in Philadelphia, and perfected the soda fountain, as known today. That was in 1825, more than a century ago. The next time you go to the drug store to imbibe a delicious chocolate soda, try to conjure a picture of Durand's store, on Chestnut Street, with its bright array of imported bottles from which he poured the flavoring extracts into the sizzling water carbonated in a machine of his own manufacture. What a quaint place that must have been!

In 1747 the attention of the scientific world was drawn to Germany, when Marggraff, a Berlin analyst, who received his inspiration and technical foundation in his father's apothecary shop, discovered that a certain type of beet contained a sugar identical with that produced from the sugar cane. In view of the great political and economic battle of tariffs, quotas and imports being waged at this very moment between the massive cane and beet sugar industries, Marggraff's discovery can be considered a major contribution to the world.

To Sweden, however, goes the honor of being fatherland to the eighteenth century's superman of pharmacy and chemistry, Carl Wilhelm Scheele (1742-1786). Scheele was a true pharmacist, having been apprenticed, according to the custom, at the age of fourteen. After having worked in a number of stores, he finally acquired his own shop and laboratory. But, regardless of whether he was in his own shop or that of an employer, he had the ability and the ambition to find time, between customers and after hours, to pursue research work along lines of original thought. One day, as he was heating together a certain mineral substance and a strong acid, he noticed a yellow-green gas which, in a few moments, made him cough violently, and almost blinded him. He knew that this was a new substance, and managed to protect his nose and eyes enough to collect some of the gas. It is known now as chlorine, although Scheele, living in the age of the phlogiston theory, called it dephlogisticated hydrochloric acid. Chlorine, as we all know, is now the basis of the

bleaching industry, is used for water purification, and has many other common uses.

On another occasion Scheele was preparing some healing plaster, and noticed that an oily liquid remained after the plaster had been completed. The substance was glycerin, which was investigated and reported upon by this Swedish apothecary, who can be said, therefore to be the founder of the great soap industry, and other industries using glycerin.

Scheele discovered prussic acid, which, as a lethal gas, is now used by the State of Utah in meting out capital punishment. Among the many famous finds credited to Scheele are the well-known tartaric, oxalic, citric and lactic acids, and the lesser used gallic, hydrofluoric and phosphoric acids, the last mentioned being obtained from bones. He was also responsible for the arsenical pigment bearing his name, Scheele's green.

They say that hard work never killed anyone. But overwork in small, cramped laboratories killed Scheele at the very early age of forty-three. Constant inhalation of gases and fumes, subjecting himself to new and untried procedures, acting virtually as a guinea pig, he passed on in the prime of life, leaving a record for industry and achievement.

Contemporary with Scheele was Martin Heinrich Klaproth (1743-1817), a German scientist who commenced his career as an apothecary. Klaproth brought to light five of the rarer chemical elements—uranium, tellurium, cerium, zirconium and titanium. These discoveries may not have founded any great industries, but they were invaluable to the progress and development of the revelation of the mysteries of chemistry.

Let us recall for a moment Marggraff's discovery of beet sugar, which, incidentally, solved a national food problem in both France and Germany.

Another apothecary helped his native France in a similar situation. During the reign of Louis XVI (1774-1792) France had a huge population. Wars, taxes and poverty were but three of the many causes of an acute food shortage, which became such a problem that the king offered a prize for a new food. Antoine Augustin Parmentier, pharmacist by appointment to His Majesty and his royal consort, Marie Antoinette, recalled his days as a prisoner of war in Germany, where potatoes were served, almost to the exclusion of other foods, at two of the three daily meals. In his native France

potatoes were looked upon as unclean, undesirable and were even reputed to be leprosy breeders. Parmentier managed to import some potatoes, planted them in a plot assigned him for the purpose, and with the crop convinced the King and the people that these "apples of the ground" make a splendid dish. Needless to say, Parmentier won the prize, with much royal recognition.

In 1797 that household medicine, the Seidlitz Powder, came into existence. The idea of placing bicarbonate of soda in one paper (blue), and tartaric acid in another (white) to be dissolved separately in water, and mixed just before using as a mild laxative, belonged to Thomas Field Savery, who patented it in 1815, with the hope of keeping the formula a secret. The secret was short lived, for in 1820, Dr. John A. Paris revealed it, along with most of the other pharmaceutical secrets of the day, in a popular book which praised the worthy proprietaries and denounced the frauds. Ah, for a book like that today, that would be read and heeded by the great medicine-guzzling public who read as they run, and who run for all the things they read about.

Sir Humphrey Davy (1778-1829), the great Englishman of all sciences, started his career as an apothecary's apprentice, training for medicine. Between the time he spent in composing and translating verses, and tinkering with mechanical gadgets, he managed to isolate a number of the elements,—sodium, potassium, magnesium, calcium, barium and strontium. He also named Scheele's dephlogisticated hydrochloric acid "chlorine." Davy's most famous work was his safety lamp for miners, which saved many lives in this hazardous occupation, and which was left unpatented by the inventor, making it easily available to all those working in the mines.

The chemical elements chromium and beryllium, and benzoic and malic acids were discovered by a French pharmacist, Louis Nicolas Vauquelin (1762-1829) who was also responsible for the discovery of the liquid alkaloid, nicotine, in tobacco. There may not be a cough in a carload, but Vauquelin proved the presence of nicotine. It is interesting to note that the term "alkaloid," applied to nitrogenous active principles of plants, was originated in 1821 by the German Apotheke Wilhelm Maissner, at Halle.

One of the most interesting of the discovery stories is that of iodine, in 1811. Once again the scene is laid in France, and, as usual, the country was at war. Napoleon was feverishly sending orders for explosives and the drug and chemical firm of Courtois and Son was

making every effort to supply the necessary nitrates. Calcium nitrate from the nitrate plantations was treated with sodium carbonate from the ashes of seaweed gathered from the nearby seashore. This formed sodium nitrate which reacted with potassium to form the desired potassium nitrate.

The younger Courtois, an observant person, noticed that the copper kettles they used for this reaction were corroded by the residue, and poured in suphuric acid in an effort to clean the kettles, and to see what caused the corrosion. Immediately intense violet vapors arose, which Courtois suspected was a new element. Pressure of business was too great to allow for any experimenting, so Courtois turned the problem over to two friends, Clement and Desormes, who established the fact that the element was iodine, and accordingly published the findings. Courtois receives full recognition as the discoverer.

Napoleon's wars and Courtois' bashful, retiring disposition cheated the latter of the discovery of morphine. Well along this road, he had to abandon the work to return to his father's drug store. Seguin and Sertürner reached the goal simultaneously, leaving Courtois far in the rear.

Friedrich Wilhelm Adam Sertürner was a German Apotheke, who, while plodding along in his little laboratory, discovered, in 1815, the narcotic principle of opium. This he very aptly called morphium, after Morpheus, the mythological god of dreams, the servant of Somnos, the god of sleep.

A short time before, in 1803, Derosne, a French pharmacist, thought that he had discovered the active principle of opium, and called it Derosne's Salt. He was wrong, however, for what he had really discovered was narcotine, which also is a misnomer, because it has no narcotic properties.

The early nineteenth century saw a brilliant partnership arrangement in the French capital. Joseph Pelletier and Joseph Caventou, Parisian pharmacists, formed a most efficient and productive scientific team, working collectively to contribute many things to the world of chemistry and medicine.

When the chills and fevers of la grippe sweep over you, what are your first thoughts? A hot bath. Quinine and whisky, of course. Pelletier and Caventou gave you the quinine, you can give yourselves the hot bath, but you are very lucky if someone gives you the whisky.

The story of quinine is one of the most romantic of the epics of medicine and pharmacy. It is of sufficient length and interest to

make, in itself, a complete popular science lecture. In brief, there was discovered, early in the seventeenth century, a Peruvian tree covered by a bark with miraculous fever-curing properties. In 1640 the Countess of Cinchon introduced it into Europe, resulting in the name,—Cinchona Bark. Many legends are connected with this bark, which was ground and taken, in its crude form, to cure various fevers. It was not until 1820 that Pelletier and Caventou very carefully and thoroughly studied Cinchona and found that it owed its curative powers to two alkaloids, quinine and cinchonine. Today we use the isolated quinine, usually in the form of the sulphate, when we wish to obtain relief from fever. For their discovey, Pelletier and Caventou received a prize of 10,000 francs from the Paris Institute of Science. This was their only reward, as they did not patent or safeguard their findings in any way.

These two accomplished men also made a very exhaustive study of the drug nux vomica, from which they extracted the principles, strychnine and brucine. Strychnine is in very widespread use today as a tonic and heart stimulant.

Pelletier and Caventou isolated caffeine, the substance that gets the blame for keeping us awake when we imbibe in a cup of coffee before retiring. At the same time, however, Robiquet, also a Frenchman, made the same discovery and received the official credit. It is frequently forgotten that Runge, a German Apotheke, had already made the discovery in 1820, but, as "fifty million Frenchmen can't be wrong," the records carry the name of Robiquet as the man who discovered the tired business man's second best friend.

Pelletier, parted for a while from Caventou, but associated with another Frenchman, Magendie, succeeded in extracting a substance from ipecac, which was called emetine. It is used today as an emetic and expectorant, and is the basis of many modern cough syrups.

Momentarily the center of the scientific stage shifted to Germany when, about 1815, the pharmacist Brandes, discovered atropine, the alkaloid of the belladonna plant, which, when taken, enlarges the pupil of the eye.

Attention was soon returned to la belle France, however, when Louis Jacques Thenard discovered hydrogen peroxide, in 1818. Thenard started his career as kitchen-boy to Vauquelin, worked his way to the chair of chemistry in the Paris Faculty of Sciences, and was made a peer in 1832.

In 1826 still another Frenchman was responsible for the discovery of still another of the elements. Antoine Joseph Balard was working in his little pharmaceutical laboratory in Montpellier, on the Mediterranean Sea, when he noticed that certain reactions on material taken from a nearby salt marsh produced a new and unfamiliar substance. Balard called it muride, from "muria," the sea, but it was later called bromos, the Greek for stench, because of its penetrating and devastating effects upon the nose and throat. It is known today as bromine.

Balard also mastered the problem of extracting sodium and potassium from the nearby ocean, but just as he had perfected the process, great natural deposits of these minerals were found in Germany, and all his work had been in vain. He made other contributions to the scientific world, especially in the field of organic chemistry, but was hampered by a carefree, almost indolent nature. Balard would rather stroll about among his friends' laboratories, assisting them and neglecting his own work. It was in this manner that he was of valuable aid to the world-renowned Louis Pasteur, originator of the science of bacteriology.

Pasteur was an apothecary at the beginning of his career, a fact very often overlooked by the chemists. Balard and Pasteur were friends, exchanging calls and assisting one another. The latter was very much engrossed in working on his ideas concerning the falsity of the current and popular theory of spontaneous generation. To prove his point, Pasteur was making cultures in a tube, but could not keep out the dirt and the dust of the atmosphere. Balard wandered in one day, sized up the situation, casually suggested that the tubes be made "S" shape, and wandered off again. Pasteur saw the wisdom of the suggestion and was able to prove his contention. There is no need for us to discuss Pasteur's great works, for they are so well known.

At about this time a few French pharmacists, led by Count Real (1815) and the Boullays of Paris (1833) first extracted the active principles from drugs by the process of percolation, passing a suitable solvent through the ground drug packed in a percolator. This process, however, never became very popular in Europe, and it remained for American druggists, such as Proctor, Squibb and Diehl to perfect and utilize the idea.

Another great advance in pharmacy was made in 1826 when Henry Hennel, in England, synthesized ethyl, or grain alcohol. Be-

fore that time fermentation of grain and other natural sources had been relied upon for the production of this very important item in chemistry and other industries. But Hennel's synthesis relegated Nature to a back seat, and made possible the statement of recent years that while there were chemists and chemistry, there could be no Prohibition.

The spotlight of pharmacy is directed now to the New World. Years before, in 1610, the first French pharmacist had reached Canada, and as we recall this, we are reminded of Willa Cather's novel "Shadows on the Rock," a wonderful, beautiful story of the apothecary in provincial Quebec. I recommend it to you, if you have not already read it. It is also significant to note that the first drug store in Boston was recorded in 1646.

But by the time about which we shall now speak, America had had its Revolution, and even its War of 1812, and had settled down to a life of constructive work. Thus, about 1835, the Philadelphia drug firm of Charles Ellis and Company had established a reputation for the manufacture of spread adhesive plaster. And the William R. Warner Company, and others, manufactured sugar-coated pills, a process half-heartedly originated sometime before by a French concern. Gelatin coating, tablet manufacturing, expert pill making and the manufacture of fluidextracts all came into vogue in this era, through the initiative and resourcefulness of the combined professional and business traits of the American druggist. As an example, Robert Shoemaker started the manufacture of glycerin in the United States in 1848, years after the Swedish Scheele had discovered it.

We must return to the Old Countries for a moment to consider a few more of their contributions. First of all, the origination, in 1837, of a solution of chlorinated soda by Labarraque, a Parisian apothecary. This solution, used as a disinfectant, is important because it is a much stronger counterpart to the very famous Carrel-Dakin Solution used so extensively in the World War in the treatment of gunshot wounds.

In 1856, Bechamp, also a French pharmacist, made an extensive study of yeast, and isolated and named zymase, the fermentation-causing principle. And so, when Rudy Vallee takes the air each week on his yeast program we can say that he owes his job to a pharmacist.

In 1857, Monsell, a fellow countryman of Bechamp, originated a salt and a solution of basic iron sulphate, official today and used as

a styptic, to treat hemorrhages. Both salt and solution bear the originator's name.

Still another countryman, Rigollet, in 1867, introduced the mustard plaster, to the chest-cold sufferers of the world. As the ads ask, "Are you a chest-cold susceptible?" If you are, you owe a debt of gratitude to Rigollet.

That seems to end the major contributions of foreign pharmacists, and our attention is focused permanently on the United States. Here was developed and elaborated the method of manufacturing compressed tablets, such as the modern aspirin tablet. Even though this idea originated in Germany in 1872, the perfection took place in America. Likewise, from about 1875 on, we can see rapid development in many other types of pharmaceutical manufacture,—enteric coating of tablets and capsules, sterilization of solutions and the dispensing of sterile solution in ampules.

In 1869, F. F. Mayer, associate editor of the *Druggists' Circular*, an American pharmaceutical trade-journal, introduced Mayer's Reagent, an alkaloidal precipitant of valuable aid in analyzing drugs. In 1872, Emil Schieffer, a German apothecary who had emigrated to America, made a careful study of pepsin and originated a process for manufacturing saccharated pepsin, thereby opening a great field of study in digestive ferments. In 1873, Joseph P. Remington, called the beloved dean of American pharmacy, introduced, as one of his many contributions, the Remington pharmaceutical still, a clever adaptation of existing principles of condensation of liquids. All of these were important additions to the medical and pharmaceutical professions.

H. H. Rusby, now Emeritus Dean of the Columbia University College of Pharmacy, has an interesting and most valuable discovery to his credit. While a student in college he evinced such great interest in botany and flowers, and all things pertaining to Nature, that he was asked to take part in an expedition into the Bolivian tropics. While there, in 1885, he heard natives' tales of the wonderful bark of a wonderful tree that induced sleep, according to them, even to those who merely reposed in its shadow. When asked to point out the tree, however, the natives always pointed farther inland. Rusby's party followed the seemingly interminable trail and finally, in Guanai, found the tree that is known today as the Guarea Rusbyi, the bark of which is known as Cocillana. This bark contains active principles producing mucous secretions when administered to humans, and in

syrup form is valuable as a cough specific. Its soothing qualities probably accounted for the exaggerated sleep stories told by the Bolivians.

Another interesting story of American pharmacy concerns Milton Franken, a Cincinnati druggist who first made yellow oxide of mercury into an eye ointment in 1892. A physician, an eye specialist, who had used Franken's ointment, was called to England to do some work, and was forced to send all the way back to Cincinnati for a satisfactory preparation of his favorite eye salve because the English pharmacists were not acquainted with the proper procedure of manufacture.

The sturdy of the well-known mercurochrome is also interesting. This antiseptic and bactericidal agent was introduced in 1919 by Hynson, Westcott and Dunning, manufacturing pharmacists of Baltimore. Used in 2 per cent. solution, this easily distinguished product produces results with little or no irritation, and, possibly, through this quality as much as any, won instantaneous success. Another triumph for American pharmacy!

Although our list is not nearly complete, for that is impossible in one hour and in a popular lecture, we have finished enumerating famous finds by pharmacists. We are ready for the summary and a conclusion. Compton's Encyclopedia says it so beautifully,—"Today the discovery of valuable remedies is not left to chance. Great drug manufacturing establishments employ experts who are constantly seeking new drugs and experimenting with their effects. How modest seem the simple mortars, retorts, and filters of the old apothecaries, compared with the equipment of the modern drug factory, with its gigantic vats, enormous distilling apparatus and power-driven pestles, crushing drugs in huge mortars!"

In an opposite view, Maurice Maeterlinck, Belgian author and Nobel prize winner of 1911, has written, "All our knowledge merely helps us to die a more painful death than the animals that know nothing. A day will come when science will turn upon its error and no longer hesitate to shorten our woes. A day will come when it will dare and act with certainty; when life, grown wiser, will depart silently at its hour, knowing that it has reached its term."

Fortunately, Science did not take that to heart. Rather, science has seemingly endeavored to refute Maeterlinck, for obviously all the efforts of the medical and pharmaceutical sciences are aimed at the prolongation of life, with the continuation of that life in health and

comfort. Life insurance company statistics clearly indicate the great lengthening of expectation of life. Childhood diseases and other ills accounting for the deaths of many of our predecessors have been totally eliminated, giving our old friends, "Natural causes" and "old age," higher scores in the mortality lists. Plagues and epidemics in civilized communities are of rare occurrence. Modern biologicals, the serums, antitoxins, the preventive medicines have all contributed to the great cause.

A healthier, more joyous life is in the very near future as researches make possible the proper combination of the ministrations of a kindly nature with advanced scientific knowledge.

Science, thank goodness, has but one fashion, according to Stedman, and that is to lose nothing once gained.

Spend a little less on alcohol, tea, coffee, tobacco and cosmetics in order to have more to spend on preventing disease and improving human health.

Try to raise the general intelligence level.

Have the courage to apply what is already known about health and disease, and to search for further knowledge along these lines.

These three pieces of advice were given to health workers of America, Canada and Mexico by Prof. Haven Emerson of Columbia University, president of the American Public Health Association, in an address before the first general session of that organization.

[Contribution From the Laboratory of Organic Chemistry of the State University of Iowa]

THE REACTION OF CERTAIN PRIMARY AMINES WITH PHENYL ISOTHIOCYANATE AND O-TOLYL ISOTHIOCYANATE

By Mina F. Goehring and Sister Mary Edward Pottebaum

IN general, aromatic primary amines add readily to aryl isothiocyanates [1] to give satisfactory yields of products that crystallize well and, in most instances, melt at convenient temperatures. Since certain of these isothiocyanates are readily available, the reaction serves for identification of the amines and furnishes a method of preparation for unsymmetrical diarylthioureas.

One purpose of this work was to obtain unsymmetrical thiocarbanilides with which to test further the observations of Walther [2] and of Raiford and Daddow [3] who noted that sym-diphenylurea, and thiocarbanilide, respectively, react with phenylhydrazine to give the corresponding semicarbazide as indicated. It was desired to include unsymmetrical compounds in further study.

$$(C_6H_5NH)_2CS + H_2NNHC_6H_5 \rightarrow C_6H_5NHCSNHNHC_6H_5 + C_6H_5NH_2$$

In the work described below it was noted that in most instances the reaction was more rapid with phenyl than with o-tolyl mustard oil, which suggested hindrance due to the methyl group.[4] When the ortho substituent was the aniline, the effect was more pronounced, but so irregular that it could not be traced to a definite cause. Thus, 2-methyl-4-nitro-,[5] 2-bromo-4-nitro-, 2,4-dinitro-, 2,6-dibromo-4-methyl-, and 2,6-dibromo-4-nitroaniline gave no thiocarbanilide, while others with no ortho substituent, such as 3,5-dibromo- and 3,5-dinitro-

[1] Weith, *Ber.*, 6, 210 (1873).

[2] Walther, *J. prakt. Chem.* (2) 53, 468 (1896); 74, 228 (1906).

[3] Raiford and Daddow, *J. Am. Chem. Soc.*, 53, 1553 (1931).

[4] Browne and Dyson [*J. Chem. Soc.*, 3287 (1931)] found that the methyl radical in this mustard oil caused pronounced inhibition in its reaction with alcohol.

[5] The observations of Meyer [*Z. physik. Chem.*, 24, 219 (1897)], Fischer and Giebe [*Ber.*, 31, 546 (1898)], and Baly and Collie [*J. Chem. Soc.*, 87, 1340 (1905)] indicate that the effect of the nitro radical is not typical of the behavior of substituents in benzene derivatives under the conditions of these and other experiments, and that the results may depend upon the chemical character of the substituent quite as much as on its position in the molecule.

anilines, did undergo the reaction but gave low yields. Steric hindrance could not account for these differences.

Experimental Part

The unsymmetrical diarylthioureas were prepared by adding to an alcoholic solution of the amine an equimolecular proportion of the isothiocyanate. When no reaction occurred within ten minutes at room temperature the mixture was heated to the boiling point for a few minutes and set aside overnight. If crystals were not present then, the treatment was repeated. The products were finally re-crystallized from alcohol. Analytical and other data are given in Tables I and II.

TABLE I

UNSYMMETRICAL DIARYLTHIOUREAS FROM PHENYL ISOTHIOCYANATE

Anilines Used (Substituents)	Yield %	M.P. °C.		Analyses			
				Nitrogen %		Halogen %	
4-Methoxy-	Nearly[a] Quant.	146[b]	Formula $C_{14}H_{14}ON_2S$	Calcd 10.85	Found 10.75	Calcd	Found ....
2,4-Dibromo-	81[a]	171	$C_{13}H_{10}N_2Br_2S$	....	....	41.45	40.94
2-Bromo-4-chloro-	61	171[c]	$C_{13}H_{10}N_2ClBrS$	....	....	33.82	33.54
2-Chloro-4-bromo-	48	170.5[c]	$C_{13}H_{10}N_2ClBrS$	8.19	8.07	33.82	34.00
2-Methyl-4-bromo-	77[a]	157–158	$C_{14}H_{13}N_2Br.S$	8.72	8.66	24.92	25.36
2-Methyl-4,6-di-bromo-	81[a]	169	$C_{14}H_{12}N_2Br_2S$	7.00	7.10	40.00	39.91
2-Methoxy-4-bromo-5-methyl-	54	150–151	$C_{15}H_{15}ON_2BrS$	....	....	22.79	22.99
2,5-Dibromo-	53	172	$C_{13}H_{10}N_2Br_2S$	7.25	7.41	41.45	41.66
2,5-Dichloro-	55	165-166	$C_{13}H_{10}N_2Cl_2S$	9.42	9.44	23.90	23.55
3,5-Dibromo-	32	163	$C_{13}H_{10}N_2Br_2S$	....	....	41.45	41.45
3,5-Dichloro-	41	155	$C_{13}H_{10}N_2Cl_2S$	....	....	23.90	23.74
3,5-Dinitro-	27[d]	190-191	$C_{13}H_{10}O_4N_4Se$	17.61	17.91	....	....
4-Phenyl-	96[a]	Indef.[f]	$C_{19}H_{16}N_2S$	9.21	9.48	....	....

a. Refers to crude yield, other values are for purified material.

b. Foerster [*Ber.*, 21, 1868 (1888)] found 127° for a phenyl anisylthiourea, the structure of which was not indicated, but which is recorded in Richter's *Lexikon* as the ortho derivative. The product listed as the p-anisyl derivative, m. p., 180°, was first obtained by Wheeler and Sanders [*J. Am. Chem. Soc.*, 22, 372 (1900)] by the interaction of phenylthioureaimidomethyl benzoate and p-anisidine, and called by them benzenylphenylthiourea-p-anisylamidine. No analysis was given. In later work [*Ibid.*, 23, 226 (1901] they claimed to have obtained the same product by the interaction of phenyl mustard oil and p-anisidine. The composition of this product rests on a single determination for nitrogen only, and the value found was seven-tenths % lower than demanded by theory.

c. A mixture of these melted without depression.

d. About 50% of starting material was recovered.

e. Composition checked by analysis for sulfur. Anal. calcd. for $C_{13}H_{10}O_4N_4S$: S, 10.06. Found, S, 10.20.

f. This behavior has previously been noted in similar products by Kjellin [*Ber.*, 36, 194 (1903)].

TABLE II

UNSYMMETRICAL DIARYLTHIOUREAS FROM O-TOLYL ISOTHIOCYANATE

Anilines Used (Substituents)	Yield %	M.P. °C.	Formula	Analyses Nitrogen % Calcd	Nitrogen % Found	Halogen % Calcd	Halogen % Found
2,4-Dibromo-	53	164	$C_{14}H_{12}N_2Br_2S$	....	....	40.00	39.91
2-Bromo-4-chloro-	90[a]	165–166	$C_{14}H_{12}N_2ClBrS$	....	....	32.48	32.45
2-Chloro-4-bromo-	52	162	$C_{14}H_{12}N_2ClBrs$	7.87	7.96	32.48	32.34
2-Methoxy-4-bromo-5-methyl-	62	159	$C_{16}H_{17}ON_2BrS$	7.67	7.87	21.91	21.99
2,5-Dibromo-[b]	26	179–180	$C_{14}H_{12}N_2Br_2S$[c]	7.00	7.10	....	....
2,5-Dichloro-	32	161–162	$C_{14}H_{12}N_2Cl_2S$	9.00	9.07	....	....
3,5-Dibromo-	31	162	$C_{14}H_{12}N_2Br_2S$	....	....	40.00	39.89
3,5-Dichloro-[d]	50	153–154	$C_{14}H_{12}N_2Cl_2S$	9.00	9.11	22.82	22.69
4-Phenyl-	96[a]	Decomp.[e]	$C_{20}H_{18}N_2S$	8.80	8.83	....	....
4-Amino-[f]	84[a]	Decomp. about 210	$C_{22}H_{22}N_4S_2$	13.79	13.98	....	....
4-(4-aminophenyl)-	92[a]	Decomp. 170–190[g]	$C_{28}H_{26}N_4S_2$	11.61	11.41	....	....

a. Represents crude yield; other values are for purified material.

b. Reaction is much more rapid in direct sunlight than in diffused daylight.

c. Composition checked by analysis for sulfur. Anal. calcd. for $C_{14}H_{12}N_2Br_2S$: S, 8.00. Found S, 7.94.

d. The only case in this study in which the reaction with o-tolyl mustard oil was more rapid than that with the phenyl compound.

e. The behavior suggests a new product and will be studied further.

f. Purified by extraction of foreign material with hot alcohol.

g. Jaffe [*Ber.*, *27*, 1559 (1894)] obtained, by the interaction of benzidine mustard oil and o-toluidine, a product that should have the structure of this one. It did not melt at 300°. Decomposition was not noted.

Summary

1. The behavior of phenyl and o-tolyl isothiocyanate toward a number of substituted primary aromatic amines has been studied.

2. In only one of the cases studied was a thiocarbanilide obtained when both ortho positions in the aniline were substituted. In comparison with this some anilines that had no ortho substituents gave low yields, and those which had the nitro radical in position 2 or 4 gave no product. Steric hindrance does not account for these differences.

3. Further work is in progress.

Iowa City, Iowa.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Arthur Osol, Ph. D.

The Determination of Phosphorus in Phosphate, Hypophosphite and Glycerophosphate Syrups. G. J. W. Ferrey.* The principle of the method depends upon the precipitation of the phosphorus as ammonium phosphomolybdate, solution of the precipitate in standard alkali and titration of the excess alkali. The reaction may be represented by the following equation:

$$2(NH_4)_3PO_4.12MoO_3 + 46NaOH = 2(NH_4)_2HPO_4 + (NH_4)_2MoO_4 + 23Na_2MoO_4 + 22H_2O$$

As each atom of phosphorus requires 23 molecules of sodium hydroxide, the amount of phosphorus required to be present for the assay is very small, of the order of 15 to 20 mgm. of phosphorus as P_2O_5. The method finally adopted was the precipitation of the phosphorus with a nitric acid solution of ammonium molybdate at 65° C., in the presence of nitric acid and ammonium nitrate; the mixture was allowed to stand at this temperature for 15 minutes, permitted to cool for another 15 minute period and then filtered. The precipitate was washed and dissolved in N/5 sodium hydroxide and titrated with N/5 hydrochloric acid, using thymol blue or phenol violet to the yellowish-green tint as indicator. This method gave excellent results, and the addition of sucrose, sodium citrate, or glycerin to the solution did not affect the assay.

Phosphate Syrups. The method was applied directly to compound syrup of ferrous phosphate, B. P., and it was found that the results could readily be duplicated and were apparently accurate. Syrup of ferrous phosphate with quinine and strychnine may also be assayed by this method if the alkaloids are first removed. This may be effected by extracting the syrup, made alkaline with ammonia, with chloroform, the aqueous solution being then assayed as before.

*Summaries of papers contributed to the Science Sessions of the British Pharmaceutical Conference, Seventy-first Annual Meeting, July 16-20, Leeds. From the *Pharmaceutical Journal*, 133, 63-93 (1934).

Hypophosphite Syrups. Compound syrup of hypophosphites B.P.C., which contains quinine and strychnine, may be assayed most conveniently by preliminary treatment with nitric acid, followed with potassium permanganate. The use of sulphuric acid should be avoided, as it leads to high results. A weighed quantity of the syrup was heated in a Kjeldahl flask with nitric acid and water, then potassium permanganate was added, and again boiled; finally, the solution was decolorized with oxalic acid and the assay completed in the usual way.

Glycerophosphate Syrups. The use of nitric and sulphuric acids for oxidation and decomposition of the glycerophosphate radical was unsatisfactory and the method was abandoned. Good results were obtained using a method of ignition. The syrup was mixed with magnesium oxide, evaporated to dryness and ignited; the white ash obtained was dissolved in nitric acid and heated on a water bath for 30 minutes, the assay being completed in the usual way. (From the Analytical Laboratory of James Woolley, Sons and Co., Ltd.)

The Preservation of Mucilage of Tragacanth. H. Burlinson.* Chloroform water is a good preservative for mucilage of tragacanth provided that care is taken to prevent the volatilization of the chloroform. In view of this disadvantage, it was decided to try other recognized preservatives, the first being the esters of para-hydroxybenzoic acid. The propyl ester (Nipasol) was found to have the most powerful preserving action. A concentration of 0.03 per cent. kept the mucilage from developing any foreign odor or taste during a period of fourteen weeks. Below 0.03 per cent., perfect preservation was not ensured.

Methyl-para-hydroxybenzoate (Nipagen) acted as a preservative in concentrations of 0.1 to 0.15 per cent. The ethyl ester was ineffective at a concentration of 0.02 per cent., but 0.05 per cent. was satisfactory. At a concentration of 0.1 per cent. the ester tended to crystallize out.

Hexyl resorcinol (Caprokol) 0.025 and 0.05 per cent. in the mucilage kept it free from fungoid growth, but on standing, the mucilage containing 0.05 per cent. and above this concentration de-

veloped a pale translucent golden yellow color, the depth of which increased with the concentration of hexyl-resorcinol.

Chlorbutol proved satisfactory in concentrations of 0.3 to 0.5 per cent. A definite camphoraceous odor and taste, however developed.

Thymol, in concentrations of 0.15, 0.03 and 0.02 per cent., was found to be quite effective as far as preserving power was concerned, but the odor and taste of the drug were perceptible.

As controls, mucilages were made using 1.25 per cent. gum in water with and without the addition of 2.5 per cent. alcohol. After standing, both developed fungoid growths, the preparations containing alcohol developing an extremely sour and fetid odor, which was less pronounced in mucilages made with gum and water only. (From the Pharmaceutical Department of Manchester University.)

The Use of Diphenylamine in the Assay of Saccharated Iron Compounds. F. Hartley and W. H. Linnell.* Determination of ferrous iron, calculated as ferrous carbonate, in saccharated carbonate of iron by titration with potassium dichromate gave the figure of 47.99 per cent. when potassium ferricyanide was used as external indicator and 51.6 per cent. when diphenylamine was used internally. The content of total iron was found to be 36.51 per cent., and that of ferric iron, by titration with titanous chloride, 13.51 per cent. The difference between these two figures gives 23.00 per cent. for the content of ferrous iron, and this is equivalent to 47.71 per cent. when calculated as ferrous carbonate; a figure which is in good agreement with that obtained by the use of potassium ferricyanide as indicator in the direct titration. It was found by varying the conditions of the determinations using diphenylamine that such variations not only affected the clarity of the end point but the actual figure for ferrous iron. In general, increase of concentration of phosphoric acid made the end point more definite, and gave a result for ferrous iron more in accord with fact. Knop's process, using definite concentrations of hydrochloric, sulphuric, and phosphoric acids was found to be most favorable, but still yielded a high result which, however, was lower than that given by the official process.

Numerous experiments directed towards the discovery of the reason for the results obtained indicated that some sugar is oxidized

during the process, but that this oxidation did not commence until after all the ferrous iron had disappeared. Thus the internal indicator which indicates the point of disappearance of ferrous iron, gave a more veracious result, whereas the diphenylamine came into operation when all the ferrous iron had been oxidized and when the rate of oxidation of the carbohydrate becomes negligible. This explains the reason why the official process yields figures which may be about 7 per cent. too high. Variations of the diphenylamine process could not yield accurate results, and thus titration with potassium dichromate using potassium ferricyanide as indicator is in every way preferable to the official process. (From the Pharmaceutical Chemistry Research Laboratory of the Pharmaceutical Society of Great Britain.)

Removal of Tattoo Marks. A simple method for the removal of tattooing was described recently in the *Münchener Medizinische Wochenschrift.* The treatment involves the use of a local application made according to the following formula:

Pyrogallic Acid		
Salicylic Acid		
Resorcinol	aa	7 Gm.
Glycerin		
Dilute Alcohol	aa	5 Gm.
Tragacanth		1 Gm.

The area around the tattooed pattern is protected by covering it thickly with zinc ointment. A piece of gauze, the size of the tattoed area, is covered with the caustic application and is applied to the tattoo in such a manner that the margin of the gauze rests on the zinc paste. The entire application is securely fixed by layers of gauze and by adhesive tape. The bandage is removed after twenty-four hours. At this time, the epidermis can be removed.

A new caustic ointment bandage is applied in the same manner as the first, but this second one is left in place for forty-eight hours. After this time, the area has usually become necrotic and only in exceptional cases does a third application become necessary. As a rule, the process is completed in from five to seven days with the marks of tattooing completely removed. (*Drug Trade News, 9,* No. 18, page 31, 1934.)

Elemental Iodine Used as Plant Insecticide. The use of iodine as an agricultural insecticide or fungicide, heretofore considered impracticable because of the danger involved to the plant host, is possible if the elemental iodine is gradually evolved by chemical action of the material sprayed upon the plant. U. S. Patent 1,964,518, issued to George M. Karns of Pittsburgh, Pa., and assigned to the Iodine Educational Bureau, Inc., of New York City, covers this invention.

It has been found that certain mixtures or substances will, upon exposure to the atmosphere, undergo slow chemical reaction, with the gradual liberation of free iodine, and that these mixtures sprayed or dusted upon plants may be used effectively and without injury to the plant to accomplish the elimination of the insects and their eggs.

Elemental iodine can be generated by iodine compounds of positive or negative valence. Where compounds of positive valence are used, they must be employed in conjunction with appropriate reducing agents; where iodine compounds of negative valence are used, appropriate oxidizing agents must be used in conjunction with them.

Among the iodine compounds of positive valence available are the following: iodates, hypoiodites and periodates. In conjunction with these, the following reducing agents may be used: sulphur and compounds of sulphur or an iodide. Iodine compounds of negative valence which are suitable include the iodides of sodium, potassium, calcium and other metals, oxidizing agents such as potassium dichromate and sodium or potassium iodate being used in conjunction with this group. (*Drug Trade News, 9,* No. 18, page 32, 1934.)

Morphine Made From Poppy Plant Waste. A new method of manufacturing opium alkaloids, recently developed in Hungary, produces morphine and codeine directly from the poppy straw remaining after the threshing of poppyseed without producing crude opium, which has always been an intermediate step in the manufacture of alkaloids. The process was developed and patented by a Hungarian pharmaceutical chemist, Janos von Kabay, and is being exploited by a factory in Budszentmihaly, Hungary, operated by the Alkaloida Company, Ltd., a firm owned jointly by the von Kabay family and the Hungarian government. During the early part of 1934 the production was at the rate of 500 kilograms of morphine annually and plans were being made to increase the capacity. The von Kabay

process yields 0.8 per cent. of morphine and 0.08 per cent. of codeine, as well as smaller quantities of other opium alkaloids. The quality of these alkaloids is said to meet the highest tests of the pharmacopœias of the United States and other countries.

In the von Kabay process, the straw is treated with an aqueous solution of a substance which dissolves the opium alkaloids. For this purpose dilute solutions of hydrochloric acid and sulphuric acid may be used. The solution is evaporated in a vacuum to one-fifth its volume and lime and alcohol are added to precipitate impurities. After filtering, the solution is again concentrated to one-fifth its volume and alcohol and sodium hydroxide are added to dissolve the morphine and precipitate other alkaloids, chiefly codeine, narcotine and narceine. To the filtrate hydrochloric acid is added and it is further concentrated until the addition of ammonia causes the morphine to separate out. (*Oil, Paint and Drug Reporter*, page 45, August 6, 1934.)

The Determination of Elemental Sulphur. H. R. Fleck and A. M. Ward. *Quart. Journ. Pharm. Pharmacol. 7*, 179-181 (1934). The weighed material, containing preferably about 0.1 gram of sulphur, is boiled in a conical flask attached to a reflux condenser with 2 grams of crystalline sodium sulphite ($Na_2SO_3.7H_2O$) and 30 to 40 cc. of water, until the sulphur has dissolved completely. By this treatment sulphur dissolves to form sodium thiosulphate quantitatively. The excess of sodium sulphite is rendered inactive by adding 10 cc. of a 40 per cent. solution of formaldehyde and 10 cc. of a 20 per cent. solution of acetic acid. After dilution to about 150 cc., the solution is titrated with N/10 iodine solution. Each cc. of N/10 iodine corresponds to 3.06 milligrams of sulphur.

The addition of 1 gram of soft paraffin, as recommended in the procedure of Allport (see *A. J. P. 106*, 67, 1934), greatly accelerated the solution in sodium sulphite reagent. The method is applicable to the determination of sulphur in flowers of sulphur, sulphur ointment, confection of sulphur, sulphur tablets and compound powder of licorice and the results compare favorably with Allport's thiocyanate method. It is reported that this method is more rapid than that of Allport.

Preparation of Iron Albuminate Solution. J. J. Vermet. *Pharm. Weekbl. 70*, 753 (1933). Through *Quart. Journ. Pharm. Pharmacol.*

7, 294 (1934). Solution of ferric albuminate is official in the Dutch Pharmacopœia, but considerable care is required to obtain a satisfactory product. It is necessary to start with a satisfactory preparation of dried egg albumin, as with many samples it is impossible to obtain a clear solution. Filtration is unsatisfactory owing to clogging, and it is best to allow the solution to settle; when, however, a sample settles out readily, it is generally found that the concentration of solids in the solution is low. The dialysis is best carried out in a shallow floating dialyser, otherwise the solution becomes too diluted. The adjustment of the strength of the dialysed solution may be conveniently based on the percentage of solids in it, instead of on the iron content. To nine parts of the dialysate, containing 6.9 per cent. of solids, one part of spirit of cinnamon is added. The iron content may then be checked, but experience shows that this always runs parallel with the percentage of solids. Determination of the spirit content by the usual method of distillation is very difficult, owing to frothing, so that it is better to control the preparation by a determination of the density. Nine parts of a dialysate containing 6.9 per cent. of solids, with the addition of one part of spirit of cinnamon, has a density of 1.009. With slightly different proportions of solids, suitable corrections may be applied.

Medicinal Ethyl Alcohol. Pure ethyl alcohol may be purchased without payment of Federal tax by

(a) any university incorporated or organized under Federal, State, or Territorial law, if such alcohol is to be used for scientific purposes;
(b) any college of learning which has a recognized curriculum and confers degrees after specified periods of attendance at classes or research work, upon proper showing of the facts;
(c) any laboratory for use exclusively in scientific research;
(d) any permanently established hospital or sanatorium in good standing, whether operated for profit or not.

To obtain tax-free alcohol it is necessary to secure a special Government permit and to give the required bond. Representatives of concerns manufacturing and selling alcohol will be glad to assist those qualified to purchase tax-free alcohol in the filling out of the requisite forms and in securing the necessary bond.

Pure ethyl alcohol, tax-paid (non-beverage) may be purchased for manufacturing purposes. No Federal permit is required for the purchase of tax-paid alcohol, but State regulations must be complied with.

SOLID EXTRACTS

Fifty years ago someone discovered that a silver dollar immersed in a glass of water, long enough, rendered the liquid not only sterile—but actually bacteriostatic.

The "Katadyn" process of sterilizing water, after three years of commercial operation now invades America, and in principle actually operates on the above-named "silver standard."

In this process the silver actually goes into solution to the extent of about one part to twenty million parts of water (about 1/300 grain per gallon) an amount certainly not calculated to do any damage. It leaves no unpleasant taste or odor and confers a long lasting germicidal action upon the water.

In Europe sterile ice that long protects foodstuffs from decomposition, vinegar, margarine, soft drinks, etc., have all been safely prepared using this Katadynized water.

The rôle of iron in the blood has been studied for many a decade. Hemoglobin, the pigment in which elemental iron seems to hold the anchor job, is a complicated molecule and in spite of the voluminous research done with it, no one yet is sure of its formula.

Where the blood stream lacks it, as in the variously caused anemias, iron in several forms, from its state in steel to its liveried comradeship with onions, have been tried to supply it. The more complicated its form the more was the hope for its success.

Recently however experimenters have concluded that the old-fashioned reduced iron and the old scale salt of ferric ammonium citrate are about the most efficacious means of administering this important element. Only they insist that large doses be given.

There is an old Welsh proverb, nearly a mile long in the original, but which when reduced to intelligible English, reads something like this, "Salt will cure all ails of the flesh, but it must be as tears or sweat or the sea."

Sea water, once thought to be but water and salt, is now said to contain a third of all the known elements in some form or another.

Actually since water is the solvent supreme, one might expect and reasonably so, that sea water contained some of every known natural element.

And more than likely the spectroscope will prove this to be so.

No sense outsenses the nose sense. Our nose knows more than we think it knows, and awakens our memories and emotions more promptly than the rest of our senses.

The amount of an odorous substance necessary to produce the sensation of smell is incredibly minute. Camphor is said to be detected in a dilution of one part in four hundred thousand, musk one in eight million, and vanillin one in ten million. Valentin found that one twenty-thousandth of a milligram (less than a millionth of a grain) of otto of rose was all that was required. Fischer and Penzoldt determined that one 460-millionth of a milligram of the rotten egg odor of ethyl mercaptan was the approximate minimum amount which, coming into contact with the olfactory nerves, could be immediately recognized by them, which is about 250 times less than the minimum amount of sodium which can be detected by the spectroscope, according to the experiments of Kirchoff and Bunsen.

The pleasant odor of the soil was ascribed by Berthelot, the distinguished French chemist, to traces of an unidentified camphoraceous body of so powerful a fragrance that even a trillionth of a milligram gave a clearly perceptible aroma.

Catnip attracts not the house cat alone but the whole fell, feline family. Purveyors and distillers of volatile oils are frequently asked for the volatile oil of catnip by hunters and trappers of the mountainous districts of the West and Southwest, who use it on the meat with which they bait their traps for mountain lions. Apparently, therefore, this odor has a special appeal not alone to the domestic cat, but to other members of the feline tribe as well.

In the Givaudanian, a pert little pamphlet dedicated to the business of "sell by smell," we came across this happy analogy.

Recently Consumers Research, Inc., issued a bulletin on perfumes and cosmetics in general, and when discussing many well-known

brands on the market selling for 50 cents, 75 cents and a dollar per unit, tried to show that the true value of these products was 3 cents, 5 cents and 15 cents per unit. The interesting part is that the Consumers Research, Inc.'s analysis is correct—in its way.

One of these days we expect a pamphlet from Consumers Research, Inc., analyzing the value of the pictures hanging in the Metropolitan Museum of Art or in the Frick Galleries. There are many pictures there which were purchased for $5,000, $10,000, $50,000 or even $100,000 each. Consumers Research, Inc., will say:

Value of frames, for instance	$15.72
Value of canvas	2.50
Paint used	7.20
Total value	$25.42

Although the above calculations may be correct, it is certain that the Metropolitan Museum would not at all feel that way about the prices it paid for its paintings. (*Givaudanin.*)

And since we are smell-bound for the moment, here is an interesting statistical item which indicates odor preference.

An advertising corporation of Milwaukee, Wisconsin, asked the opinions of a large and intelligent group on a list of fifty-five different smells. The questionnaire was simple and direct. All it requested in the case of each odor was that the voter should indicate whether he liked, disliked or was neutral (indifferent) to it. The odors preferred, in order of choice, taking only the first 10, were: (1) rose (85 per cent.), (2) pine (83), (3) lilac (83), (4) violet (77), (5) lily-of-the-valley (77), (6) coffee (76), (7) balsam (76), (8) cedar (73), (9) strawberry (68), (10) wintergreen and apple (67). Those disliked, arranged similarly were: (1) perspiration (97 per cent.), (2) garlic (92), (3) rubber (81), (4) lard (79), (5) kerosene (77), (6) olive oil (70), (7) fish (70), (8) onion (66), (9) turpentine (63), (10) gasoline (59).

MEDICAL AND PHARMACEUTICAL NOTES

DAKIN'S SOLUTION—BY ELECTROLYSIS. Dakin's solution, wartime antiseptic for treating infected wounds, may now be easily and satisfactorily made by an electrolytic cell. The apparatus was designed by Dr. O. R. Sweeney of Iowa State College at Ames, and has been developed for practical use in hospitals by Paul A. Frank of Akron, Ohio.

Dakin's solution, invented by Drs. H. D. Dakin and M. Daufresne during the early days of the World War, is a relatively unstable, 0.5 per cent. solution of sodium hypochlorite. Since the war its use in civilian hospitals has been limited by its poor keeping qualities and the fact that it requires considerable skill in its preparation and administration. If it is not strong enough it will not destroy the microorganisms in the wound, and if too strong it will injure the tissues of the body. The differences between being too strong and not strong enough is very small.

To overcome the technical difficulties in preparing this solution, Dr. Sweeney designed a simple, practically foolproof apparatus which is now called the antiseptic cell. An electric current controls the chemical reaction so that the resulting solution is of just the right strength. The hospital technician has only to put into the apparatus a measured amount of sodium chloride, distilled water and sodium bicarbonate, and turn on a switch. Fresh hypochlorite solution is then automatically produced at the rate of about an ounce a minute. (*Science News*, September 8, 1934.)

SODIUM SALICYLATE AND BICARBONATE, DISCOLORATION OF MIXTURES CONTAINING. M. Beukema-Goudsmit. (*Pharm. Weekbl.*, 1934, *71*, 196.) The discoloration which occurs in mixtures containing sodium salicylate and sodium bicarbonate is due to oxidation by atmospheric oxygen, and is increased by the use of the sesquicarbonate in place of bicarbonate. On the other hand, the presence of sodium hydroxide causes very little discoloration which is therefore not due to the *p*H of the solution. Very small amounts of calcium

salts completely prevent the development of the color, so that it does not appear if tap water is used, or even water which has been boiled with calcium carbonate. (G. M. through *Quart. Jour. Brit. Pharm. Conf.*)

BLOOD MEDICATION—BY SKIN. Certain medicines are more effective in treating diseases of the blood vessels when induced to enter the body by the aid of an electric current than when given by mouth or by hypodermic injection under the skin, a group of Columbia University physicians has found.

Acetyl-beta-methyl choline hydrochloride is the remedy experimented with although histamine and cystine derivatives are likely to act in a similar fashion. The first named has been found useful in treating Raynaud's disease and certain other ailments, including chronic arthritis, because it improves the local circulation.

When this medicine or similar ones are given by mouth they have little or no effect. When given by injection under the skin or into the muscles, the action is very transient because the medicine is quickly destroyed by the blood. When injected directly into the veins it is highly poisonous. But given by what the doctors call galvanic induction through the skin, its effects are more prolonged and hence more satisfactory, they found.

While the treatment is not a "cure" for rheumatism or chronic arthritis, it gives striking results, reducing the swelling, increasing the general activity of the joints without pain and making the patient more comfortable.

An asbestos bandage soaked in the medicine is wrapped around the affected limb or joint. Over this is placed a flexible metal plate which is connected to the positive pole of a galvanic generator. A moist pad electrode placed on the back is connected to the negative electrode and the current turned on and slowly increased. The electric current breaks the medicine down into ions which are carried into the skin.

It might be exceedingly interesting to study the absorption of the antisyphilitics mercury and bismuth by this same method.

ACTION OF SUNLIGHT AND NORMAL SUMMER TEMPERATURE

Variations on Odor Values of Extracts in Flint and Amber Glass Bottles

	Flint Bottles		*Amber Bottles*	
	1 month's exposure	*2 months' exposure*	*1 month's exposure*	*2 months' exposure*
Vanilla	Noticeable deterioration in odor value	Noticeable deterioration in odor value	N. C.	N. C.
Orange	Noticeable deterioration in odor value	Appreciable deterioration in odor value	N. C.	Slight deterioration in odor value
Lemon	Marked deterioration in odor. Brown sediment	Quite disagreeable off-odor	N. C. No sediment	Slight deterioration in odor value
Cinnamon	N. C.†	N. C.	N. C.	N. C.
Strawberry	N. C.	N. C.	N. C.	N. C.
Anise	N. C.	Slight deterioration in odor value	N. C.	N. C.
Cherry	N. C.	N. C.	N. C.	N. C.
Imitation Onion	Disagreeable off-odor Cloudy	Disagreeable off-odor Cloudy	N. C.	N. C.
Wintergreen	N. C.	N. C.	N. C.	N. C.
Imitation Pistachio	Off-odor	Off-odor	N. C.	N. C.
Clove	N. C.	N. C.	N. C.	N. C.
Imitation Banana	N. C.	N. C.	N. C.	N. C.
Imitation Maple	Faint change in odor value	Faint change in odor value	N. C.	N. C.
Lime	Slight off-odor	Slight off-odor	N. C.	N. C.
Rose	N. C.	Slight off-odor	N. C.	N. C.
Almond	Off-odor, cloudy and slight sediment	Disappearance of Almond odor. Sediment	N. C. Clear. No sediment	
Pineapple	N. C.	Appreciable deterioration of odor	N. C.	N. C.
Raspberry	Much weaker in odor value	Much weaker in odor value	Slightly weaker in odor value	Slightly weaker in odor value
Nutmeg	N. C.	N. C.	N. C.	N. C.
Peppermint	Off-odor	Off-odor	N. C.	N. C.
Mint	N. C.	Slight deposit Distinct camphoraceous odor	N. C.	N. C.

† N. C. No change.

—(*The American Perfumer.*)

SUN TAN FILTERS

Ingredient	*Filtering effect on skin*	*Fluorescence*
White petrolatum	good	bluish-white
Yellow petrolatum	excellent	bluish-white
Mineral oil	fair	dark blue
Peanut oil	fair	dark blue
Coconut oil	fair to good	dark blue
Calamin ointment N. F.	excellent	brick red
Calamine lotion	excellent	brick red
Benzyl salicylate	excellent	deep blue
Phenyl salicylate	excellent	deep blue
Methyl anthranilate	excellent	bright bluish-white
Phenyl-ethyl anthranilate	excellent	bright bluish-white
Linalyl anthranilate	excellent	bright bluish-white
Iso-butyl anthranilate	good	bright blue
Linalyl methyl anthranilate	good	bright blue
Terpenyl anthranilate	fair	deep blue
Methyl methyl anthranilate	fair	deep blue
Balsam Peru oil, syn.	excellent	deep blue
Sulfonated olive oil	good	yellowish-green
Oxyquinoline sulfate 1:500	good	deep red
2-napthol-3, 6, disulfonic acid	good	bright bluish-white
Sodium-2-naphthol-6-8-disulfonic acid	good	bluish-white
Quinine bisulfate	good	bright blue
Quinine oleate (25% quinine)	good	yellowish-brown
Aesculin	good	bright bluish-white
Turtle oil	fair to good	bluish-green
Lanolin	excellent	yellowish
Olive oil	fair	yellowish-green
Corn oil	fair	bluish-green
Avocado oil	fair	yellowish-green
Passion fruit oil	fair	greenish-blue
Methyl coumarin	good	bluish-white
*Picric acid ½%	——	blood-red
*Esters p-oxy-benzoic acid	——	blue
Menthyl salicylate	excellent	bluish-white
Amyl salicylate	good	bluish-white

*Not tested on the skin.

It will be noted that there are a number of odoriferous oils or liquids contained in the above table. They are recommended as aromatic ingredients. It would seem that a 5 per cent. quinine oleate ointment in wool fat and scented with the grape esters should provide excellent skin protection.

DETERGENTS FOR CHINA AND GLASSWARE

Sodium metaphosphate	48	parts
Trisodium phosphate	18	"
Sodium metasilicate	28	"
Sodium hydroxide	6	"

All are the dehydrated salts.

This mixture, recently studied, under a Mellon Institute Fellowship, is claimed to be the superior of any in the large or small-scale cleansing of china and glassware.

"And the trail of medical history today runs true with its typical, eccentric, erratic course.

"Serums, endocrines, vaccines, surgical tricks—ectomy this, otomy that—transfusions, infusions, delusions, adjustments, psychopaths, allopaths, neuropaths, homeopaths—the regular paths and a few detours.

"The pet of today is the pest of tomorrow, and the dregs of yesterday are the drugs of today.

"Indications of the times seem to point to a renaissance of botanical medicine. Somewhere in the Scriptures it is mentioned that the green things that grow shall be a healing balm to ease humanity's aches and pains. And too long have these been neglected. So truly as the Peruvian bark has furnished the specific to dread malaria and the white poppy of India its soporific juice, equally true is it that there are myriad useful plant antidotes to pain waiting for proper appraisal."—(*Internat. Clinics.*)

BOOK REVIEW

THE MERCK MANUAL OF THERAPEUTICS AND MATERIA MEDICA. A source of ready reference for the physician. Sixth Edition Fabrikoid. 1397 pages. Price, $2. Compiled and published by Merck & Co., Inc., Rahway, N. J.

This edition, the sixth and outstanding Edition of a well-known and favorably accepted publication, not only has been enlarged and thoroughly revised, but contains many interesting new features. Unique and refreshing is the ready reference which may be made to this publication during busy professional hours, when neither time nor expediency permit of extensive library consultation. In the therapeutic portion of the more than thirteen hundred pages, two hundred and fifty-seven pathological conditions are presented alphabetically, with reference to etiology, diagnosis and therapy. Over two thousand prescription formulas chiefly covering official constituents with metric system equivalents, are provided. These are arranged in numerical sequence with reference to the use of each in therapy. The discussion on therapy is an interesting departure in a book of this type and is a favorable contrast to the stereotyped presentations frequently encountered in more extensive treatises. There is the constant reminder that the patient as well as the disease is being treated, and that general regimen, diet and psychotherapy are not merely accessories, but frequently fundamentals in practical therapy. In line with contemporary medical progress, there have been included, many important subjects such as the reclassification of Anemia, the therapy of Myasthenia Gravis, the elucidating differential diagnosis of Uremia, Dyspnea, and others, contained in the various tables. The chapters on Pneumonia, Pain, Diabetes, Nephritis, Shock and Collapse, in themselves, would justify the publication of this *vade mecum.*